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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/045,230	11/09/2001	John Tallman	99,130-H	3200

7590 02/23/2006

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EXAMINER	
BRANNOCK, MICHAEL T	
ART UNIT	**PAPER NUMBER**
1649	

DATE MAILED: 02/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/045,230	TALLMAN ET AL.	
	Examiner	Art Unit	
	Michael Brannock	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-35 and 51-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-35 and 51-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *none* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *062705*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application: Claims and Amendments

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1649.

Applicant is notified that the amendments put forth on 6/23/05, have been entered in full.

Response to Arguments

Applicant is notified that the finality of the prior Office action (mailed 4/19/05) is withdrawn in view of Applicant's persuasive arguments.

Maintained Rejection:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 24-35 and 51-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6444666, filed August 27, 1998 in view of Mohler-H et al. Neurochemical Res. 20(5)631-636, 1995.

The invention of the instant claims is predicated on the idea that selective activation GABAA alpha 2 receptors and/or alpha 3 receptors, while minimizing activation of receptors having alpha 1 subtype, will produce anxiolytic effects with minimal sedative and cognitive impairing effects, see pages 33-39.

U.S. Patent 6444666 teaches this concept at col 2, lines 20-24. The patent appears to be silent with regard to screening methods however the artisan would immediately envision such screening methods. In fact, it is inherent in the identification of the compounds of the patent that screening methods must be employed in order to determine the selectivity of the disclosed compounds. Thus, although the patent does not teach any particular *in vitro* efficacy value or EC_{50}, e.g. that the EC_{50} be less than 200 nM as in the instant claim 24. One of ordinary skill in the art of pharmacology would not need to be taught what particular numbers to use as this would readily be apparent during routine optimization of operating parameters. Further, claims 34, 35, and 54 require the additional steps of measuring the selectivity *in vivo* and the patent does not discuss this. However, as the object of the proposed assay is to identify agents that would be useful for *in vivo* use, it would be obvious to one of ordinary skill in the art to additionally measure the *in vivo* efficacy using the old and well established models of anxiety and sedation.

Additionally, U.S. Patent 6444666 does not specifically teach which beta and gamma subunits should be used in the assays. In Table II of Mohler it is taught that the naturally occurring configuration of GABAA receptors having the alpha 2 or alpha 3 subunits are each complexed with the beta 3 and gamma 2 subunits. Therefore, one of ordinary skill in the art, at the time the invention was made, and with reasonable expectation of success, would be motivated to use beta 3 and gamma 2 subunits when practicing the claimed invention suggested

by U.S. Patent 6444666, because such configurations are taught by Mohler to be found in nature, as any artisan would appreciate that the naturally occurring configurations would provide the greatest likelihood of identifying physiologically relevant compounds.

Applicant argues that U.S. Patent 6444666 (Ladduwahetty) teach only binding assays not functional assays as required by the claims; and that the instant specification teaches that binding assays wrongly identify antagonists as well as the required agonists. This argument has been fully considered but not deemed persuasive as it is premised on an unreasonably poor view of the level of skill of one of ordinary skill in the art of receptor pharmacology, which is quite high. First, Ladduwahetty specifically state that at col 2, line 65: "Desirably, the compounds of the invention will exhibit functional selectivity in terms of a selective efficacy for the alpha-2 and/or alpha-3 subunit relative to alpha-1 subunit. One of ordinary skill in the art would fully and immediately appreciate that this statement directly refers to and encompasses the functional assays referred to by Applicant and widely known and practiced in the art.

Applicant points to the Paul Whiting article as providing evidence that the skilled artisan would only know to conduct conventional screening assays based on binding affinity upon reading the Ladduwahetty patent. This argument has been fully considered but not deemed persuasive Whiting is providing a general review of the art of GABAA receptor study and, in the statement referred to by Applicant, Whiting is actually contrasting the study of GABAA receptors with traditional methods of studying receptors in general. That is, summing-up what is known in the art, Whiting indicates that functional studies of GABAA receptors are most important, see col 1 of page 652. Whiting reviews the art of functional assays of GABAA receptors and points to two references [13,14] (page 648) that were published a decade before

Ladduwahetty filed for their patent. Thus, the desirability and routine nature of functional assays of GABAA receptors was old and well established in the art at the time Ladduwahetty patent was filed. As this was well appreciated by Ladduwahetty, the patent states the desirability of functional assays but does not go into great detail as these are well known in the art. In fact, contrary to Applicant's assertion, and apparently escaping the examiner's notice as well, functional assays involving cloned and transfected host cells are taught by Ladduwahetty at col 8 Lines 46-63 and *in vivo* animal assays are taught beginning at line 64.

Conclusion

Please note the new central fax number for official correspondence below:

No claims are allowable.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX months.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Brannock, Ph.D., whose telephone number is (571) 272-0869. The examiner can normally be reached on Mondays through Fridays from 10:00 a.m. to 4:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, Ph.D., can be reached at (571) 272-0867. Official papers filed by fax should be directed to **571-273-8300**.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

MB

July 27, 2005

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER